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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/750,846	01/05/2004	Heimo Haikala	06267.0116	3865

22852 7590 09/27/2006

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EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/750,846	HAIKALA ET AL.	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3 and 5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *May 30, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

CLAIMS 3 AND 5 ARE PRESENTED FOR EXAMINATION

Applicants' Amendment, Terminal Disclaimer and Information Disclosure Statement filed May 30, 2006 has been received and entered into the application. Accordingly, claim 3 has been amended; claim 4 has been canceled; and claim 5 has been added. Also, as reflected by the attached, completed copy of form PTO/SB/08, (1 sheet)[1], the Examiner has considered the cited references.

The Terminal Disclaimer is in proper form. Accordingly, the double patenting rejection of claims 3 and 4, as set forth in the previous Office action dated January 27, 2006 at pages 5 and 6, is *withdrawn*.

Applicants' remarks concerning the propriety of objecting to claims 3 and 4 as incomplete, (i.e., see the amendment at page 3), have been considered. While not in agreement that the issue raised by the Examiner should not be corrected, upon further consideration the objection is *withdrawn*. The issue concerning the propriety of claiming a reduction in mortality which is not associated with congestive heart failure will be more appropriately evaluated under 35 U.S.C. § 112, first paragraph, *infra*.

The references newly cited by the Examiner and not relied on herein have been included to show the general state of the art.

Claim Rejection - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

[1] The sheet indicated that it was sheet "1 of 2". A second sheet, however, could not be found. Accordingly, the Examiner changed the page numbering to indicate "1 of 1".

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing mortality resulting from congestive heart failure in a patient suffering therefrom, does not reasonably provide enablement for reducing the mortality, in general, of a patient suffering from congestive heart failure. As the presently claimed subject matter reads on reducing the mortality from *any* cause in a patient suffering from a certain disease, i.e., here it is congestive heart failure, where the mortality and the disease are not associated, such reads on extending the lifespan of such a patient beyond his/her normal expected lifespan, where the patient would otherwise die from a cause or causes that is/are not necessarily associated with the heart failure. The specification, however, does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In order to overcome the present rejection, Applicants may wish to consider amending the claims to read "A method for reducing mortality resulting from congestive heart failure in a mammal suffering from congestive heart failure, comprising administering...".

Burden on the Examiner for Making a Rejection Under 35 U.S.C. § 112 First Paragraph

As set forth in *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971):

"[A] [s]pecification disclosure which contains teaching of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with enabling requirement of first paragraph of 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contain therein which must be relied on for enabling support*; assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in specification is truly enabling." (emphasis added).

Further, the following excerpts from the MPEP at section 2164.04 are deemed germane:

- "According to *In re Bowen*, 492 F.2d 859, 862-63, 181 USPQ 48, 51 (CCPA 1974), *the minimal requirement* is for the examiner to give reasons for the uncertainty of the enablement."(emphasis added).

- "While the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) (a.k.a. the "Wands Factors" as delineated in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) and the evidence as a whole, ***it is not necessary to discuss each factor in the written enablement rejection***. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims."(emphasis added).

Here, the Examiner is addressing the following "Wands Factors" in order to support his conclusion that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims: (1) breadth of the claims; (2) the state of the prior art; (3) the lack of predictability; (4) the amount of direction provided by the inventor; and (5) the existence of working examples.

State of the Art and Lack of Predictability Therein

Concerning the breadth of the instant claims, The present claims recite "A method for reducing mortality in a mammal with congestive heart failure...". A nexus between the mortality and the heart failure has not been included. There, a broad and reasonable interpretation of the claims

include a method for extending the lifespan of the mammal suffering from congestive heart failure in instances where the mortality could be caused by events unrelated to the heart failure, e.g., dying from blunt force trauma sustained in a automobile accident or from "natural causes". In order to achieve the objective of the claims, it is required that the (R)-enantiomer of N-[4-(1, 4, 5, 6-tetrahydro-4methyl-6-oxo-3-pyridazinyl)phenyl]acetamide, or salts thereof, (hereinafter "compound I") is administered to the mammal in an effective amount.

As per the Court's direction in *Marzocchi*, cited above, the objective truth that mortality from any and all causes could be reduced, which may also be interpreted as extending the lifespan of a subject, by simply administering compound I to the subject is doubted by the Examiner because the art (see the references relied upon *infra*) establishes that lifespan extension may be accomplished by only a particular means. The claims do not include such means.

In particular, Roth et al. (European Journal of Clinical Nutrition; newly cited by the Examiner) teaches "Dietary energy restriction is ***the only proven method*** for extending lifespan and slowing aging in mammals, while maintaining health and vitality"(emphasis added) (the abstract at page S15, first sentence) and Roth et al. (Annals New York Academy of Sciences; newly cited by the Examiner) teach "Dietary caloric restriction (CR) is the *only* intervention conclusively and reproducibly shown to slow aging and maintain health and vitality in mammals" (abstract at page 305, first sentence).

Thus, the art recognizes only calorie restriction in mammals for extending the lifespan thereof and Applicants' implicit contention is conspicuously inconsistent with contemporary wisdom in the art of lifespan extension. Based upon the teachings of the art, it would therefore be unpredictable that the lifespan of mammals could be extended by ingesting compound I.

Examples/Guidance of the Specification

In the present specification there are no examples of having a mammal's mortality reduced or lifespan extended through the administration of compound I, where such mortality is shown to be caused by a representative number of events that would be indicative of the genus "mortality" presently claimed. In Applicants' Figure 1, blood levels of levosimendan and compound I are shown. Also, "the Kaplan Meier" curves for "all cause" mortality is shown in Figure 2. Further explanation of the significance of this example has not been provided.

Lacking such evidence, and in light of the state of the art, the Examiner is compelled to conclude that the specification is enabling only for a method of reducing mortality caused by congestive heart failure in a patient suffering from heart failure which comprises administering compound I to said mammal.

Summary

As the cited art and discussion above establish, practicing the claimed method in the manner disclosed by Applicants would not imbue the skilled artisan with a reasonable expectation that the mortality of a mammal suffering from congestive heart failure, or any other disease, could be reduced through the administration of compound I, where such mortality is not caused by or associated with congestive heart failure. In order to actually achieve the claimed objective in the claimed host with compound I, it is clear from the discussion above that the skilled artisan could not rely on Applicants' disclosure as required by 35 U.S.C. § 112, first paragraph. Given that the art fails to recognize and Applicants have failed to demonstrate that mortality in general could be reduced in a mammal suffering from congestive heart failure, the

skilled artisan would be faced with the impermissible burden of undue experimentation in order to practice this embodiment of the claimed invention.

Accordingly, claims 3 and 5 are properly rejected.

Legal Standard for Anticipation/Inherency Under - 35 USC § 102

To anticipate a claim under 35 U.S.C. § 102, a single prior art reference must place the invention in the public's possession by disclosing each and every element of the claimed invention in a manner sufficient to enable one skilled in the art to practice the invention. *Scripps Clinic & Research Foundation v. Genetech, Inc.,* 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1001 (Fed. Cir. 1991); *In re Donahue,* 766 F2d531, 533, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985). To anticipate, the prior art must either expressly or inherently disclose every limitation of the claimed invention. *MEHL/Biophile Int'l Corp. v. Milgraum,* 192 F.3d 1362, 1365, 52 U.S.P.Q.2d 1303, 1303 (Fed. Cir. 1999) (citing to *In re Schreiber,* 128 F.3d 1473, 1477, 44 U.S.P.Q. 1429, 1431 (Fed. Cir. 1997)); *Atlas Powder Co. v. Ireco Inc.,* 190 F.3d 1342, 1347, 51 U.S.P.Q.2d 1943, 1946 (Fed. Cir. 1999). To inherently anticipate, the prior art must necessarily function in accordance with, or include, the claimed limitations. *MEHL/Biophile,* 192 F.3d at 1365, 52 U.S.P.Q.2d at 1303. However, it is not required that those of ordinary skill in the art recognize the inherent characteristics or the function of the prior art. *Id.* Specifically, discovery of the mechanism underlying a known process does not make it patentable. See also MPEP §§ 2112, 2112.02 and 2145(II).

Multiple Reference 35 U.S.C. § 102 Rejection

This Office action contains a rejection under 35 U.S.C. § 102 based on multiple references. The additional reference is relied on to explain the meaning of a term used in the

primary reference or to show that a characteristic not disclosed in the primary reference is inherent. Accordingly, the Examiner's reliance on multiple references is proper. "Normally, only one reference should be used in making a rejection under 35 U.S.C. § 102. However, a 35 U.S.C. § 102 rejection over multiple references has been held to be proper when the extra references are cited to:

(A) Prove the primary reference contains an "enabled disclosure;"

(B) Explain the meaning of a term used in the primary reference; or

(C) Show that a characteristic not disclosed in the reference is inherent." (See MPEP § 2131.01).

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Verheugt FWA: Hotline sessions of the 21st European Congress of Cardiology. Eur. Heart J. (1999) 20:1603-1606.

Verheugt teaches the treatment of congestive heart failure patients with an effective amount of levosimendan, as compared to an effective amount of dobutamine. The reference reports that "The primary end-point was reached in 28% of the levosimendan patients at 24 h vs 15% of dobutamine patients (P=0·022). By 24 h no patient on levosimendan had died compared

to three deaths in the dobutamine group. At 180 days following infusion, these figures were 26% and 38%, respectively (P=0·03). Apparently, in patients with sever congestive heart failure requiring intravenous inotropic support, a 24 h infusion of levosimendan is superior to dobutamine in the early and medium term outcome. The relatively high mortality with dobutamine may constitute an adverse effect of dobutamine, whereas the long-term effects of levosimendan are promising.".

While the reference does not specify the presently claimed compound I, such would have been inherent in the prior art method because, as acknowledged by Applicants at page 1, the final three lines.

Accordingly, the claims are deemed properly rejected.

Claim Rejection - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 3 and 5 are rejected under 35 U.S.C. 103(a) as being obvious over Haikala et al. (U.S. RE38,102, "Haikala '102"), Haikala et al. (U.S. Patent No. 5,905,078; "Haikala et al. '078") or Applicants' acknowledgment at page 1, lines 2-4 of the third paragraph, **or** Sircar (U.S. Patent No. 4,397,854) in view of Campbell (U.S. Patent No. 4,432,979) and Diamond et al. (U.S. Patent No. 4,517,310), each of record, for the reasons of record as set forth in the previous Office action at pages 2-4, as applied to claims 3 and 4, which reasons are here incorporated by reference, in further view of Verheugt.

Applicants' remarks and the references submitted to the Office have been carefully considered, but fail to persuade the Examiner of error in his determination of obviousness.

In particular, Applicants have urged that one of ordinary skill in the art would have known that that positive inotropic therapy for congestive hear patients has *caused* mortality in such patients and thus, the artisan would not have expected a mortality reducing effect for the presently claimed compound I. In support of the position that inotropic therapy was known to cause mortality, Applicants rely on an article by Kasper and a review article by Katz.

The Examiner, however, is not persuaded because given the evidence of record in support of the present rejection, it is not clear that compound I was recognized as being an inotropic agent whose actions mirrored the inotropes known at that time. In fact, from the newly cited Verheugt article, it would appear that one would have expected that the present compound I was not detrimental to mortality in congestive heart failure patients. Also, Applicants have not pointed to and provided a necessary explanation of the evidence relied on for support of their contention that the "mortality reducing effect of compound (I) in congestive heart failure patients was unexpectedly found in the clinical trials conducted by the applicants", (amendment at page 6). Further, it is not clear that the mortality to which Applicants refer is commensurate in scope with the present claims, i.e., the claims encompass mortality caused by any and all causes and not only from congestive heart failure.

Accordingly, for the above reasons, the claims are deemed properly rejected.

None of the claims are currently in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Raymond J Henley III
Primary Examiner
Art Unit 1614

August 6, 2006